Central Asian Journal of Nephrology
(eISSN 3105-4145)

Editorial

Development of Nephrology Research in Central Asia and Beyond

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Abstract:

Received: August 20, 2025
Accepted: August 23, 2025

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It is with great honor and enthusiasm that I present to you the first issue of the Central Asian Journal of Nephrology (CAJN). This new journal comes at a critical time for the region, when the burden of chronic kidney disease (CKD), acute kidney injury and associated comorbidities is steadily increasing, while systematic research and evidence-based methods, as well as the development and implementation of new technologies, remain limited. Our mission is to create a dedicated platform for knowledge sharing, collaboration and policy development aimed at improving kidney health in Central Asia and beyond.

Introduction

Regional context

Central Asia occupies a unique geographical and cultural position, linking East and West, tradition and innovation. The countries of this region - Kazakhstan, Kyrgyzstan, Uzbekistan, Tajikistan, Turkmenistan and neighboring states - are united not only by geographical proximity, but also by deep genetic, cultural, educational and social similarities. These common characteristics have a profound impact on the epidemiology, clinical course, and treatment effectiveness of kidney disease.

Lifestyle factors such as diets high in salt and animal fats, high rates of hypertension and diabetes, and environmental exposures contribute to the high prevalence of CKD in the region. Moreover, genetic predispositions shaped by centuries of common ancestry and migration may underlie specific kidney pathologies but remain poorly understood. Despite these common features, most of the scientific evidence underlying current nephrology practice is derived from studies of West or East Asian populations, which do not fully reflect the regional realities of Central Asia.

The need for research and collaboration

The lack of region-specific data makes it difficult for clinicians and policymakers to develop effective prevention, screening, and treatment strategies. Although the burden of kidney disease is evident in hospital wards and dialysis centers across Central Asia, much of it remains unrecorded in global health statistics and ignored in international research programs.

With the Central Asian Journal of Nephrology, we aim to change this situation. We see the journal as a catalyst for collaborative research, bringing together nephrologists, internists, epidemiologists, geneticists, public health experts, and policymakers. By publishing original research, reviews, clinical cases, and practical recommendations, CAJN will become an important repository of knowledge that reflects the realities of our population.

Furthermore, the journal aims to promote regional integration of research. Kidney disease knows no political boundaries, and neither does our research. By pooling resources and expertise across Central Asian

countries, we can conduct multi-center studies, establish registries, and develop locally relevant guidelines that can transform practice.

Global contribution

Although the journal focuses on Central Asia, its implications extend far beyond the region. Global nephrology can benefit from understanding the interplay of genetic predisposition, cultural traditions, and environmental factors that shape kidney health in our populations. Knowledge gained in Central Asia can shed light on global issues such as diabetic nephropathy, glomerular diseases, and the impact of climate and environmental change on kidney disease outcomes.

Moreover, as our region is at the crossroads of civilizations, it has the potential to bring together different scientific traditions and bring unique ideas to the global nephrology community. We aim to provide an inclusive platform where international scientists can interact with their Central Asian counterparts, enriching the dialogue and advancing common solutions.

A look into the future

The launch of the Central Asian Journal of Nephrology marks more than the birth of a new scientific journal – it is an effort to raise the profile of kidney health on the regional and global agenda. We call on clinicians, researchers and policymakers to join us in this endeavor: collecting data, publishing results, engaging in dialogue and, ultimately, improving the lives of millions of people living with kidney disease.

On behalf of the editorial board, I thank all the authors, reviewers and partners who supported this concept and contributed to the implementation of this first issue. Together, we have the opportunity to shape the future of nephrology in Central Asia and thereby make a significant contribution to the development of global healthcare.

We are pleased to welcome you to the Central Asian Journal of Nephrology, a journal born in Central Asia but whose voice and influence extends far beyond its borders.

The Kidney Fund of Kazakhstan has taken such an important responsibility to create this international platform and the opening of the Central Asian Journal of Nephrology, and we are open to cooperation and affiliation with other professional societies, global pharmaceutical companies, higher education institutions and research institutes in Central Asia and beyond.

Central Asian Journal of Nephrology
(eISSN 3105-4145)

Original Article

Cardiovascular Diseases in Dialysis Patients at Different Levels of Healthcare of the Republic of Uzbekistan

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Received: June 11, 2025
Accepted: June 20, 2025

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Abstract:

Background: Despite the fact that the prevalence of CKD and its effects on health have been studied mainly in economically developed countries, the burden of this disease is even greater in developing countries. It has been established that more than 50% of deaths in patients with ESRD are due to cardiovascular causes. The objective of our study is to comparatively study the structure of cardiovascular diseases in dialysis patients at different levels of health care in Uzbekistan.

Methods: 165 dialysis patients (90 men and 75 women) were studied. The main initial diseases were chronic glomerulonephritis (n=76), diabetes mellitus (n=44), urolithiasis (n=14), chronic pyelonephritis (n=10), etc. Patients were included from 3 clinics of different administrative levels - republican (n=32), urban (n=72) and rural (n=61).

Results: CVDs were identified in 69% of the urban, 44% of the regional and 47% of the republican population. In the structure of CVD, AH, IHD and CHF prevailed in all groups. Also, in the groups of the republican and city level, CVD was more common in a combined form, while dialysis patients at the regional level had more isolated CVD pathology.

Conclusion: Patients of the urban population on dialysis more often suffer from CVD than patients receiving HD at the republican and regional levels of health care. The combined lesion of the CVS occupies a leading place in the structure of CVD in dialysis patients at both urban and national levels.

Keywords: Cardiovascular Diseases; CKD; Hemodialysis; Hypertension; Coronary Heart Disease; Heart Failure

Introduction

Globally, the total number of people with chronic kidney disease (CKD), acute kidney injury (AKI) and those receiving renal replacement therapy (RRT) exceeds 850 million, which is indeed twice the estimated number of people with diabetes worldwide and 20 times higher than the number of people with acquired immunodeficiency syndrome (AIDS)/human immuno-

deficiency virus (HIV) worldwide (1). According to international guidelines (2), it is recommended to consider all patients with CKD as individuals with an increased risk of developing cardiovascular diseases (CVD), with level of evidence 1A.

The guidelines of the Russian Society of Cardiology "Cardiovascular risk and chronic kidney disease: cardio-nephroprotection strategies" (2013) prescribe mandatory determination of the state of renal function by glomerular filtration rate (GFR) and/or urinary albumin excretion (3). Epidemiological studies indicate a high incidence of cardiovascular disease (CVD) in patients with (CKD) (4, 5). Thus, the prevalence of arterial hypertension (AH), as the most important risk factor for coronary heart disease (CHD) and left ventricular hypertrophy (LVH), in chronic kidney disease is 87-90%. While in the general population, the prevalence of AH is less than 40%. At least 35% of patients with renal pathology at the time of contacting a nephrologist have various manifestations of CHD in their history (myocardial infarction or angina). The presence of CHD at the start of renal replacement therapy (RRT) increases the risk of death on hemodialysis by 45%, and heart failure - by 93% (6). Most patients with CKD do not develop progressive or end-stage kidney disease (ESRD), but they have an increased risk of cardiovascular disease (CVD) (7). The risk of CVD increases inversely with the level of GFR, and at GFR <30 ml/min it exceeds that with preserved renal function by 5.5 times. A significant number of patients with CKD die due to CVC even before ESRD (8).

Studies have shown that mortality from CVD in dialysis patients is 10-20 times higher than in the general population (9). S.H. Chung et al. reported that the risk of mortality for dialysis patients with CVD was 3.3 times higher than for non-smoking dialysis patients without CVD (10). In the study of J. Tong et al., mortality among dialysis patients with CVD was 2.9 times higher than that in other patients (11). There are works in the literature devoted to CVD in patients with CKD 5D, however, they are mainly devoted to the study of any one of the pathologies of the heart and blood vessels, while a comprehensive assessment of the frequency, structure and comparative assessment of CVD in dialysis patients at different levels of health care are not presented (12, 13).

Despite the fact that the prevalence of CKD and its impact on health have been studied mainly in economically developed countries, the burden of this disease is even greater in developing countries (14), which show the relevance of studying this problem in our country.

The purpose of this work is to comparatively study the structure of cardiovascular diseases in patients with terminal CKD receiving program hemodialysis at different levels of health care in the Republic of Uzbekistan.

Methods

Participant Selection: A total of 165 patients (90 men and 75 women) with stage 5 CKD undergoing program hemodialysis were examined. The study included patients with a clinically established diagnosis of stage 5 CKD as a result of nephropathies of various origins. GFR was calculated based on serum creatinine concentration using the CKD-Epi formula. The main underlying diseases were chronic glomerulonephritis (n=76), diabetes mellitus (n=44), urolithiasis (n=14), chronic pyelonephritis (n=10), etc. The duration of HD was 29 (6-89) months. Programmed hemodialysis was performed using Fresenius Medical Care 4008S devices, WEGO F15 LW and Diacap Polysulfone LOPS18 LW dialyzers. Hemodialysis sessions were performed according to the scheme of 4 hours 3 times a week (12 hours/week) according to international recommendations. Bicarbonate solution was used as a dialysate for hemodialysis. Kt/V indicators corresponded to the minimum target level of 1.4. The criteria for exclusion from the study were age under 18 years, patients who underwent kidney transplantation, patients receiving HD for acute renal failure (Figure 1).

Study Design: This study is an original prospective cohort study. The study was performed in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committees of all participating clinical centers. Written informed consent was obtained from all participants before inclusion in the study.

In order for the study to represent the entire spectrum of patients from hospitals of different administrative levels, the cohorts included all patients from each of the three hospitals who were on program hemodialysis at the time of the initial examination. Patients were included from 3 clinics of different administrative levels - republican (n = 32), city (n = 72) and rural (n = 61). The studies were conducted at the Republican Specialized Scientific and Practical Medical Center of Urology (republican level), the City Nephrology Hospital of

Tashkent (city level) and the Syrdarya Regional Multidisciplinary Medical Center of Gulistan (rural level).

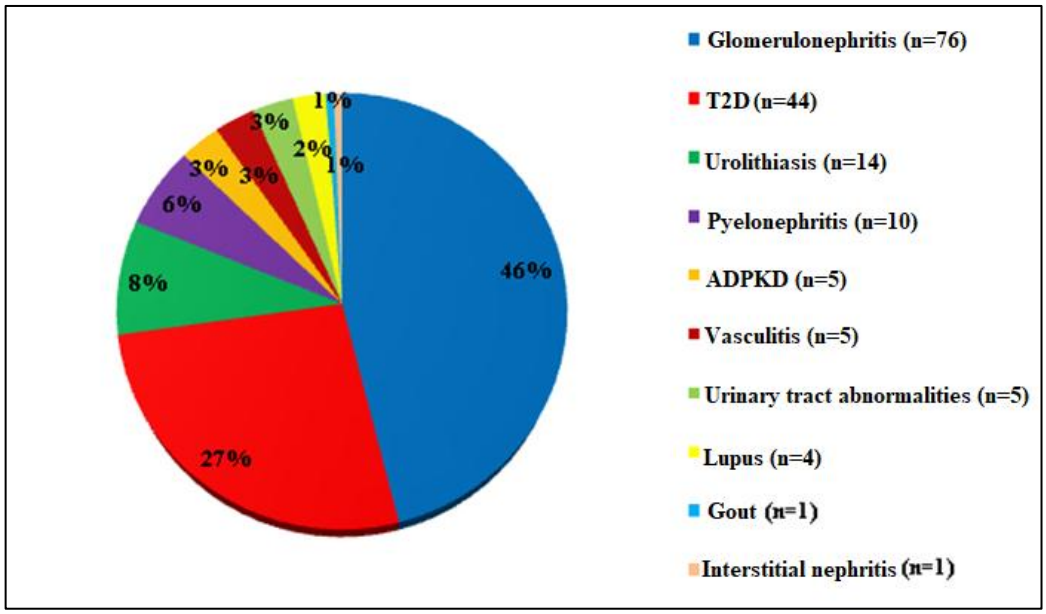

Figure 1. Etiology of CKD 5D in the studied patients (n=165).

The distribution of patients by gender and age in the groups who took part in the study is shown in Table 1. As can be seen from the table, if in general there was no clear predominance of male patients (54.5% (n=90) of all those examined were men, 45.5% (n=75) were women), then in the rural group there was an almost twofold excess of men over women: 39 (64%) and 22 (36%) patients, respectively.

Table 1. Distribution of patients with CKD 5D by sex and age (M±m).

Indicator	Republican level	City level	Rural level	All patients
All patients, %	32 (19 %)	72 (44 %)	61 (37 %)	165 (100 %)
Men, %	16 (50 %)	35 (49 %)	39 (64 %)	90 (54,5 %)
Women, %	16 (50 %)	37 (51 %)	22 (36 %)	75 (45,5 %)
Average age, years	51,2±2,65	49±1,62	45,5±1,83	48,1±1,11
Average age of men, years	48,8±3,68	48,1±2,3	44,6±2,30	46,7±1,49
Average age of women, years	53,6±3,83	49,9±2,29	47,1±3,06	49,9±1,66

The age of the patients ranged from 18 to 78 years. The average age was 48.13±1.11. The patients at the republican level were aged from 27 to 78 and had an average age of 51.2±2.65 years. The patients at the urban level were younger, their average age was from 18 to 78 and was 49.0±1.62 years. The rural group of patients was the youngest, from 18 to 69. Their average age was 45.5±1.83 years.

Data Collection & Variables: All patients underwent laboratory and instrumental examination upon inclusion in the study, including general blood and urine tests, biochemical blood tests (total protein, azotemia

indicators), electrocardiography, ultrasound examination of the kidneys, echocardiography (Table 2).

Table 2. Main indicators of dialysis patients at different levels of health care (M±m).

Parameters		Republican level	City level	Rural level
Sex	men(%)	16 (50 %)	39 (64 %)	35 (49 %)
	women(%)	16 (50 %)	22 (36 %)	37 (51 %)
Average age, years		51,2±2,65	45,50±1,83	49,00±1,62
Average duration of HD, months		58,40±12,28**	16,60±2,40†	27,40±3,79§§
SBP, mmHg		133,90±4,71	140,90±2,47	148,60±3,09§
DBP, mmHg		84,30±2,44	89,20±1,50	86,80±1,54
HR, bpm		80,80±0,95	80,90±0,94	80,40±1,13
Total blood protein, g/l		70,70±1,10***	62,90±0,87†††	65,70±0,93§
Hemoglobin, g/l		92,10±3,78***	73,30±2,19	85,80±2,30§§§
Erythrocytes, *1012/l		3,00±0,13*	2,70±0,06	2,8±0,70
Blood urea, mmol/l		25,00±2,88*	18,00±1,10	23,80±0,89§§§
Blood creatinine, μmol/l		637,20±44,03	604,40±40,44	705,00±28,27§
GFR (according to CKD-Epi), ml/min		8,8±0,88	11,5±1,34	7,6±0,58§§

*Note: the reliability of the difference is indicated by symbols: between the groups Republic and Region - *, Republic and City - ^, Region and City - Δ(for */†/§, p<0.05, for **/††/§§, p<0.01, for ***/†††/§§§ p<0.005).*

Statistical Analysis: Statistical data processing was performed using the standard Statistica for Windows package, version 6.0. The Mann–Whitney test was used to compare two independent groups, the Kruskal–Wallis test was used to compare more than two independent groups, and the Spearman test was used for correlation analysis. Multiple linear regression analysis was also performed. Differences were considered reliable at $p<0.05$.

Ethical Considerations: Example: "All participants provided written informed consent.

Results

According to our study, the structure and frequency of CVD differed in patients of the 3 groups both in structure and frequency (Table 3).

When examining the data obtained, the indicators of the rural and republican levels are noteworthy. In these groups, the frequency of cardiovascular diseases did not differ significantly from each other and amounted to 44% and 47%, respectively. At the same time, at the urban level, the frequency of CVD at the start of the survey was 1.5 times higher than both the rural and republican levels, amounting to 69% (Figure 2).

Table 3. The structure and frequency of cardiovascular diseases in patients with CKD 5D.

Parameters	Republican level (n=32)	City level (n=72)	Rural level (n=61)
Total patients with CVD	15 (47 %)*	50 (69 %)†††	27 (44 %)
Total patients with AG	15 (47 %)	45 (62,5 %)††	24 (39 %)
Total patients with CHD	3 (9 %)***	39 (54 %)†††	5 (8 %)
Total patients with CHF	1 (3 %)***	19 (26 %)†††	3 (5 %)
Total patients with arrhythmia	-	5 (7 %)	3 (5 %)
Including:			
with AG + CHD	2 (6 %)***	24 (33 %)†††	2 (3 %)
with AG + CHF	-	3 (4 %)	1 (2 %)
with CHD + Arrhythmia	-	2 (3 %)	1 (2 %)
with AG + CHD + CHF	1 (3 %)	10 (14 %)†	1 (2 %)
with AG + CHF + Arrhythmia	-	-	1 (2 %)
with AG+CHD+CHF+Arrhythmia	-	3 (4 %)	-

*Note: the reliability of the difference is indicated by symbols: between the groups Republic and Region - *, Republic and City - †, Region and City - § (for */^/§, p<0.05, for **/^^/§§, p<0.01, for ***/^^^/§§§ p<0.005).*

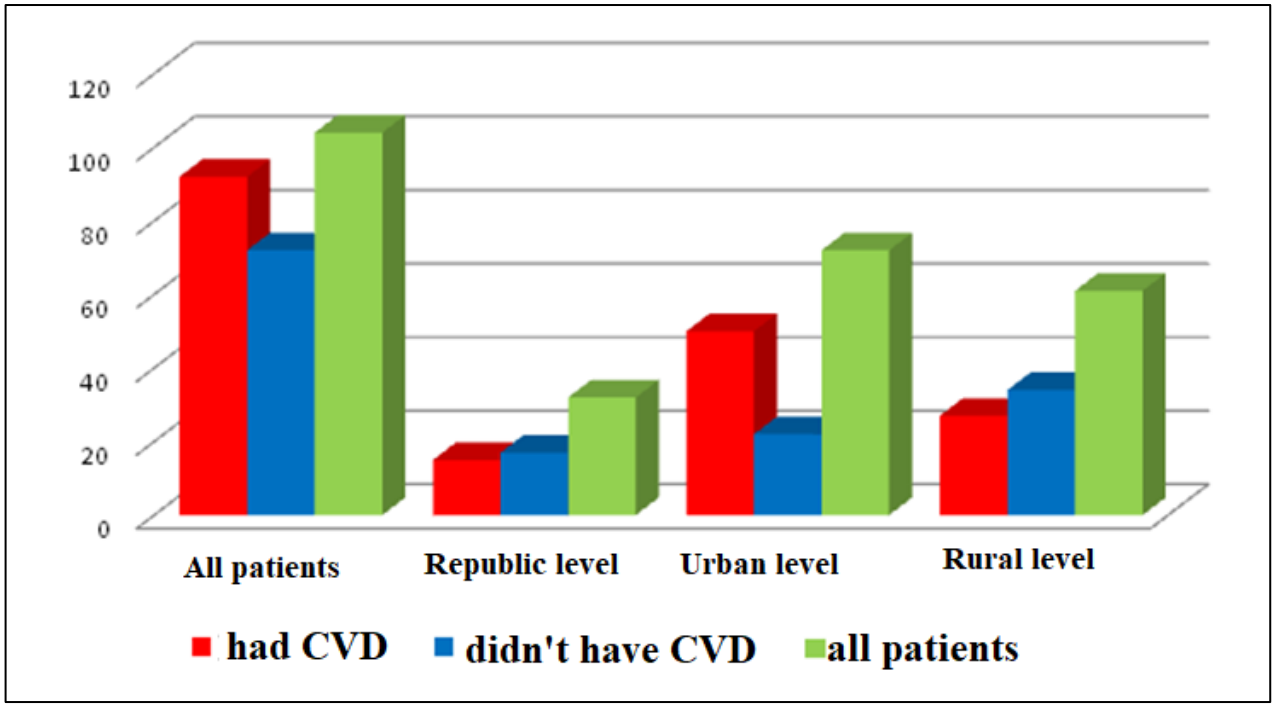

Figure 2. The ratio of patients with CVD and without CVD in groups.

Depending on gender, the incidence rates of CVD in all groups did not differ significantly (Figure 3).

We examined the frequency of CVD separately in each group of patients. At the same time, a number of features were revealed, which is associated with the status of the medical institution.

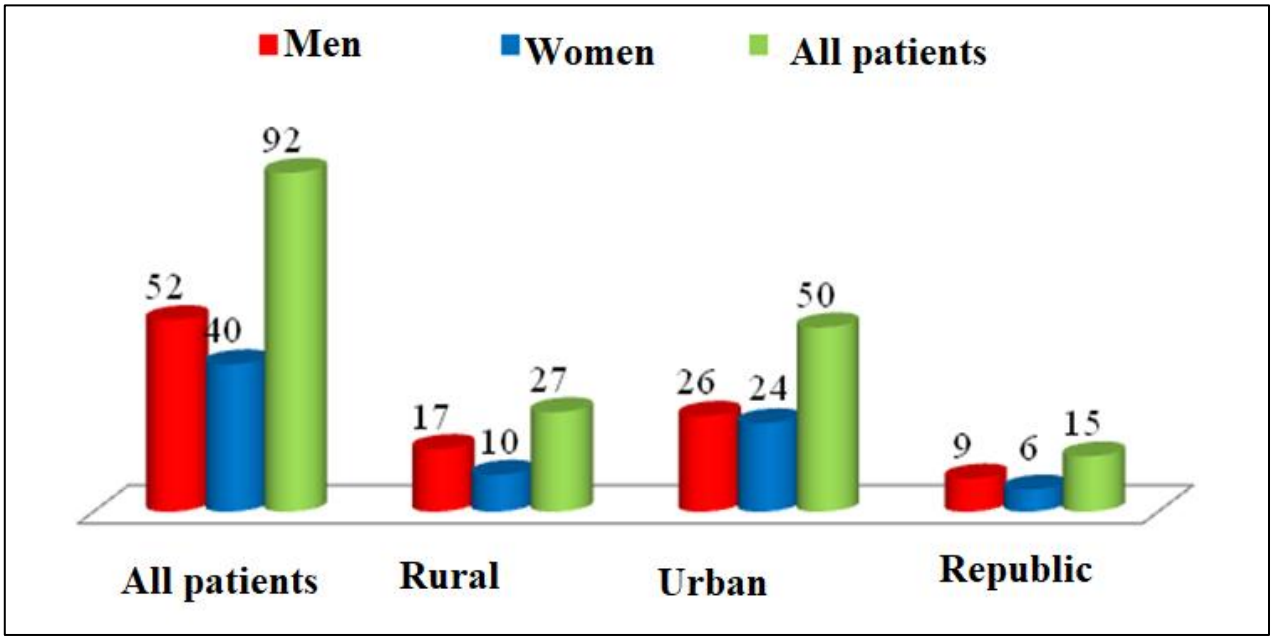

Figure 3. Sex ratio of patients with CVD.

In the urological center (republican level), 47% of patients were diagnosed with some CVD. At the same time, all examined patients (n=15) were found to have hypertension, both isolated and in combination with other CVD diseases. The majority (n=12) of patients had isolated hypertension. In 3 patients, hypertension was combined with coronary heart disease, and in 1 case, with the development of heart failure with combined hypertension + coronary heart disease (Figure 4). A feature of this group of patients was the absence of patients with coronary heart disease and arrhythmia.

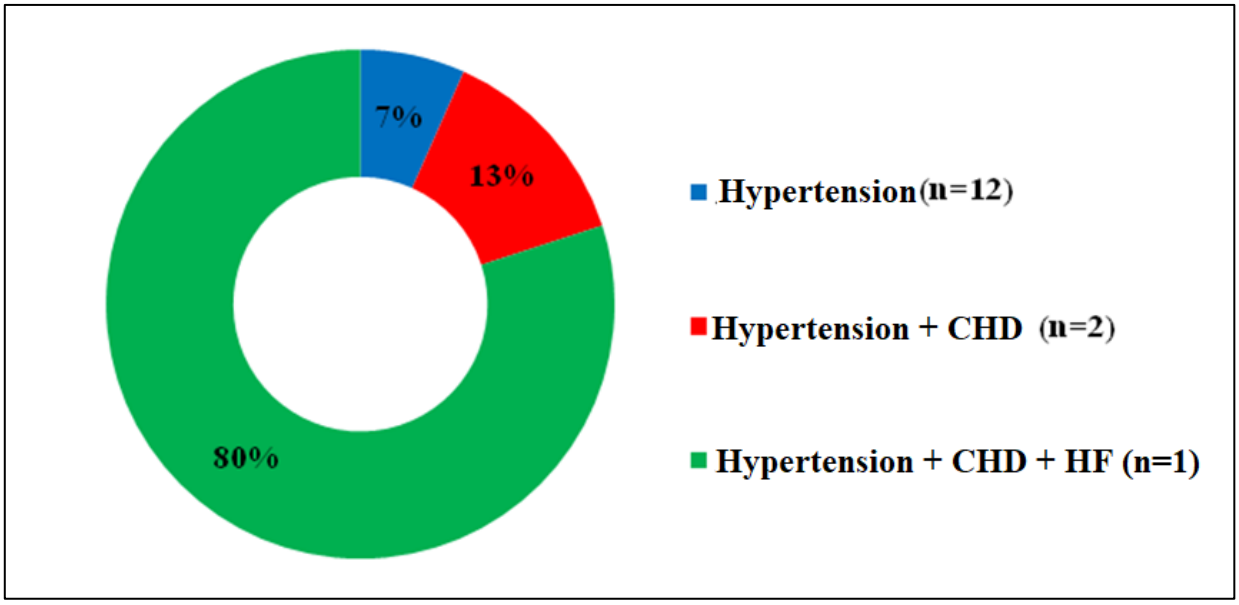

Figure 4. The structure of cardiovascular diseases in dialysis patients at the republican level (n=32).

At the city level, CVD was detected in 50 patients (69%). Here, the most common CVD was hypertension, it was found in 62.5% (n=45) of all patients. At the same time, this group also had a significant frequency of patients with coronary heart disease (54.2%, n=39) and CHF (26.4%, n=19). The most common combination of CVD was hypertension + coronary heart disease. It was found in almost half (n=24) of patients with CVD in the city. A feature of this group of patients was the high frequency of combined cardiovascular diseases as a complication of hypertension and coronary heart disease - 59.7% (n=43) in various combinations (Figure 5).

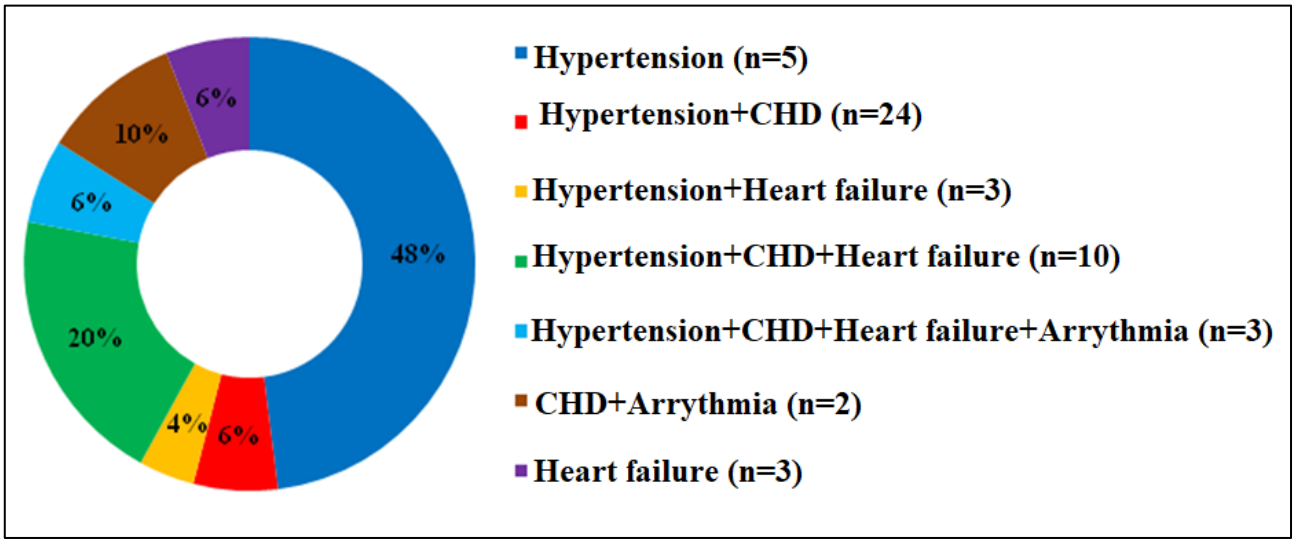

Figure 5. Structure of cardiovascular diseases in dialysis patients at the city level (n=72).

Another feature of this group of patients was the high frequency of diabetes. In 50 patients with CVD, diabetes was diagnosed in 48% (n=24) of cases. It should also be noted that anemia was highly prevalent in this group of patients - it was found in 47 (94%) patients with CVD. These data indicate not only the actual frequency and structure of comorbid conditions in patients with CKD 5D in the urban population, but also their better detection in this institution. At the rural level, CVD was detected in 44.2% (n=27) of patients. We have already mentioned two reasons for such a low detection rate of CVD. As in other institutions, hypertension was the most common CVD pathology in patients on HD - 39% (n=24) of all patients. This amounted to 89% of all CVD in this group. The frequency of coronary heart disease (n=5), CHF (n=3) and cardiac arrhythmia (n=3) was almost the same. The combination of CVD was also represented by isolated cases (Figure 6).

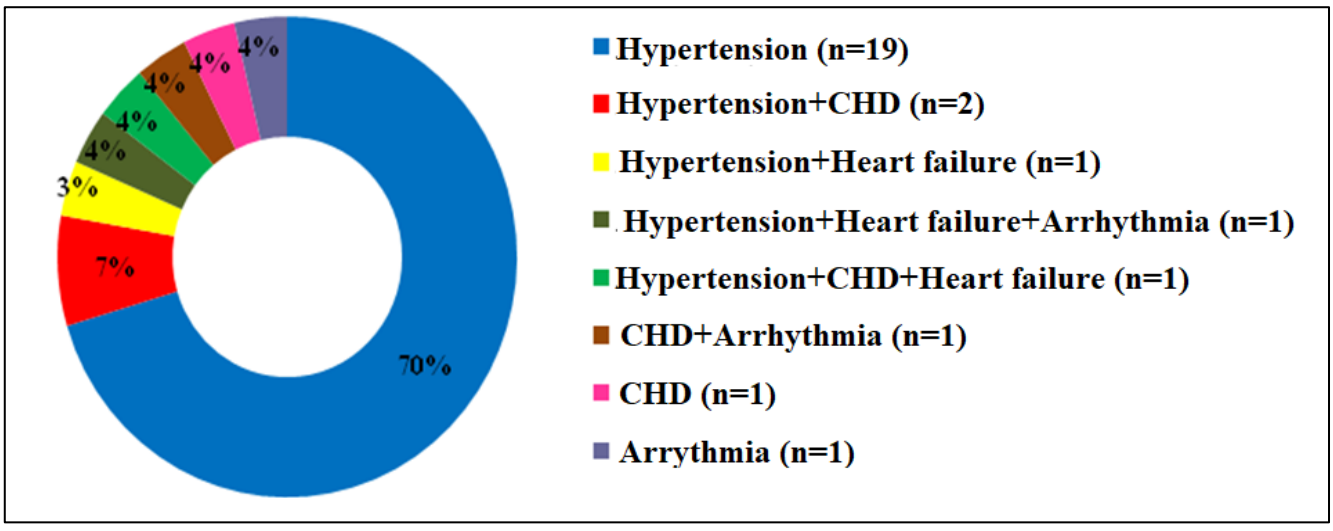

Figure 6. Structure of cardiovascular diseases in dialysis patients at the rural level (n=61).

At the rural level, 77% (n=47) of all examined patients had anemia, and in patients with CVD, anemia was found in 70% of cases (in 19 of 27 patients). 11 (41%) of 27 patients with cardiovascular diseases suffered from diabetes.

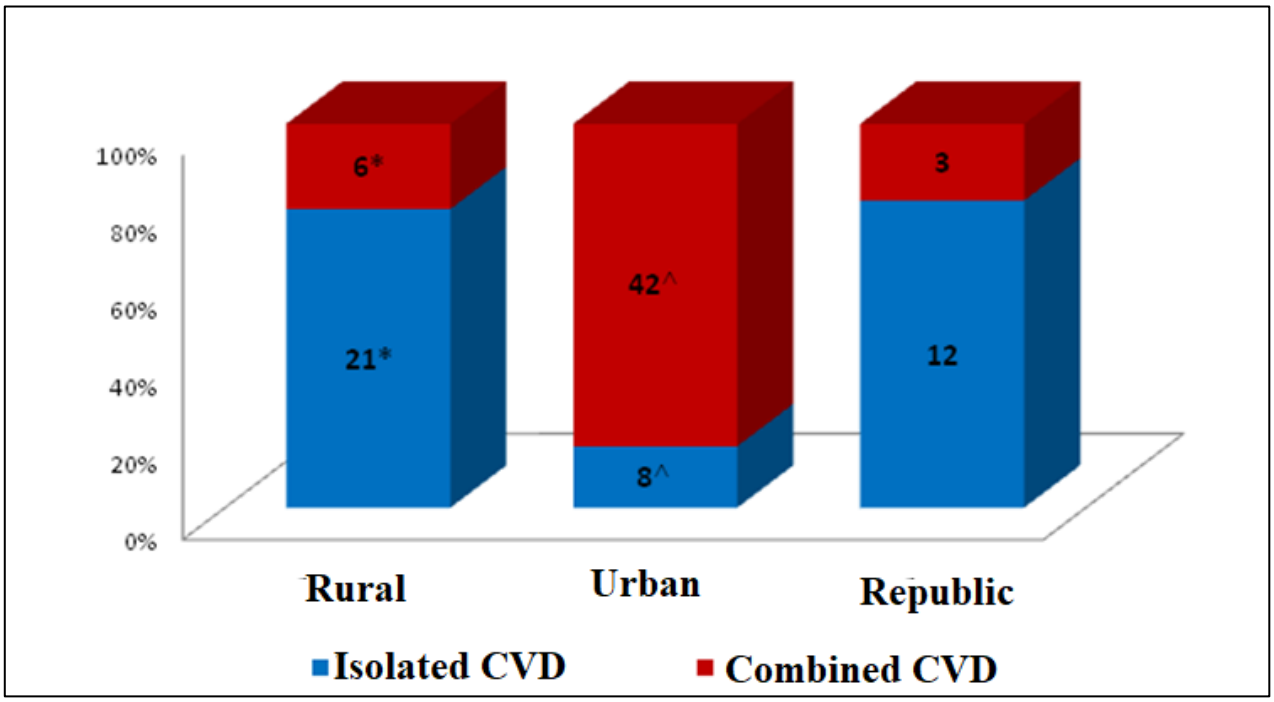

Figure 7. The ratio of patients with isolated and combined pathologies of the cardiovascular system in the study groups.

*Note: p <0.05 is indicated by symbols: between rural and urban groups - *, city and republic - ^, region and republic - Δ*

As noted above, the structure of CVD was presented both in an isolated form and in combined CVD lesions. Moreover, at the republican and rural levels, combined CVDs accounted for 20% (n=3) and 22% (n=6), respectively, while at the urban level this figure was 84% (n=42) (Figure 7). This indicates the fact that the urban contingent had a greater comorbidity in CVD, which is a risk of cardiovascular mortality in patients with CKD 5D.

Discussion

According to our study, the structure and frequency of CVD had significant differences in patients in 3 centers of different levels of healthcare in the Republic of Uzbekistan. When considering the obtained data, attention is drawn to the indicators of the rural and republican levels. In these groups, the frequency of CVD did not differ significantly between themselves (44% and 47%, respectively). At the same time, in the city, the frequency of CVD at the beginning of the survey was 1.5 times higher than the indicators of both the rural and republican levels, amounting to 69%. In our opinion, this is due to a number of objective and subjective reasons. First of all, this is due to the characteristics of the contingent applying to medical centers of different levels. In the city, mainly residents of Tashkent apply, living in conditions of high urbanization, fast pace of life, psychoemotional overload and a sedentary lifestyle, contributing to the development of CVD. Numerous studies have proven that residents of large cities are more susceptible to CVD (15, 16). At the same time, at the republican level, all patients were also residents of Tashkent, but in this group, the low frequency of CVD was associated with the specificity of a specialized urology center and a specific contingent of patients with a urological profile.

In rural population, a lower frequency of CVD is associated, on the one hand, with the fact that patients living in rural areas, less susceptible to coronary heart

disease, come here. On the other hand, patients had coronary heart disease and hypertension not diagnosed in primary health care. In addition, an analysis of diagnoses in case histories showed that patients before and during HD were given a detailed diagnosis associated with kidney pathology, while not in all cases CVD was reflected in concomitant diseases by nephrologists. They reflected easily detectable hypertension and arrhythmia in the diagnosis of this contingent of patients.

In urban patients, 69% of patients were diagnosed with CVD. Of these, the most common CVD was hypertension - 62.5%. At the same time, a significant frequency of patients with coronary heart disease (54.2%) and chronic heart failure (26.4%) was also noted in this group. A feature of this group was a high frequency of combined cardiovascular diseases - 59.7% and diabetes. In 50 patients with CVD, diabetes was diagnosed in 48% of cases. The high incidence of anemia indicates not only better detection of comorbid conditions in this institution, but also their real frequency and structure in patients with CKD 5D in the urban center.

The prevalence of combined CVD lesions shows that at the urban level there is a high comorbidity for CVD, which is a high risk of mortality in patients with CKD 5D. These data were confirmed in the analysis of mortality in patients at the urban level. It turned out to be the highest compared to the rural and republican center.

These data in practical terms force us to reconsider the strategy for managing these patients in favor of a strict system of prevention and treatment of CVD, which has significant prospects for increasing survival and further referral for kidney transplantation.

Conclusion

Dialysis patients often (in 44-69% of cases, depending on the level of healthcare) have comorbid CVD pathology. Based on the analysis of 165 dialysis patients, regardless of the level of medical care, the main CVD pathologies in patients were hypertension, coronary heart disease and CHF. According to the results of our study, patients with stage 5 CKD at the urban level suffer from CVD more often than at the republican and rural levels. Combined CVD pathology occupies a leading place in the structure of CVD in patients with stage 5 CKD at the republican and city levels of healthcare. In the gender context, the structure of CVD did not differ significantly between the groups.

Author Contributions: Conceptualization, B.D.; methodology, B.D., O.S.; writing – original draft preparation, B.D., O.S.; writing – review and editing, B.D., O.S. All authors have read and agreed to the published version of the manuscript.

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: None.

Ethics approval: Not applicable

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Central Asian Journal of Nephrology
(eISSN 3105-4145)

Review Article

Toward Precision Medicine in Diabetic Kidney Disease: The Call for Integrative Genomic Research in Kazakhstan

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Abstract:

Diabetic kidney disease (DKD) is a major complication of diabetes mellitus and the leading cause of end-stage renal disease (ESRD) worldwide. Despite considerable research efforts, the pathogenesis of DKD remains incompletely understood, largely due to its multifactorial etiology and pronounced phenotypic heterogeneity. Genome-wide association studies (GWAS) have identified over 40 loci associated with DKD; however, these common variants collectively explain only a small fraction of the disease's heritability. Rare and low-frequency variants, often undetected by GWAS, are increasingly recognized as important contributors, and next-generation sequencing (NGS) technologies offer valuable tools for their identification. Kazakhstan, characterized by a unique genetic landscape and substantial ethnic admixture, remains underrepresented in DKD genomics research. Expanding integrative, high-resolution genomic studies in such settings is essential for identifying population-specific risk variants, improving diagnostic accuracy, and advancing precision medicine approaches to DKD prevention and management.

Received: June 19, 2025
Accepted: June 23, 2025

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Keywords: Diabetic Nephropathy; Diabetes Mellitus; Genome-Wide Association Study; Next-Generation Sequencing; Single Nucleotide Polymorphism; Genetic Susceptibility Loci

Diabetic kidney disease (DKD) is a major complication of diabetes mellitus (DM) and the leading cause of end-stage renal disease (ESRD) worldwide (1). DKD develops in approximately 30% of individuals with type 1 diabetes mellitus (T1DM) and in about 40% of those with type 2 diabetes mellitus (T2DM), contributing to a substantial socioeconomic burden on global healthcare systems (2).

The pathogenesis of DKD is highly complex and remains incompletely understood, contributing to ongoing controversies in its clinical management and unsatisfactory patient outcomes. DKD development and progression are driven by a multifactorial interplay of interrelated mechanisms, including hemodynamic and metabolic dysregulation, oxidative stress, activation of the renin–angiotensin–aldosterone system (RAAS), chronic systemic inflammation, and progressive fibrosis (3-5). Notably, the incidence and severity of DKD exhibit considerable ethnic and geographical variation, with markedly higher rates observed in individuals of African descent (three- to six-fold greater), as well as among Mexican Americans and Pima Indians (6). This marked heterogeneity suggests that both modifiable risk factors, such as poor glycemic control, severity of metabolic disturbances, dietary patterns, and socioeconomic conditions, and non-modifiable factors, particularly genetic predisposition and disparities in healthcare access, may collectively influence disease

susceptibility (7). A growing body of clinical evidence supports the role of inherited genetic variants in conferring individual risk for DKD (8).

Several genetic strategies have been used to identify risk loci and genes, including candidate gene analyses, family-based linkage analysis, transmission disequilibrium testing, population-based admixture mapping, and genome-wide association studies (GWAS) (9). The field of human genetics has been revolutionized by the Human Genome Project, which provided a complete map of the human genome and laid the foundation for large-scale genetic association studies (10). GWAS have advanced the identification of common genetic variants contributing to complex diseases, including DKD. GWAS through agnostic scanning of millions of single-nucleotide polymorphisms (SNPs) across the genome have identified 41 loci associated with DKD at genome-wide significance across diverse populations globally (8).

According to a GWAS meta-analysis involving up to 19,406 European individuals with T1DM, 16 loci reached genome-wide significance in association with DKD, with four loci of particular interest located within or adjacent to kidney-function genes, *COL4A3*, *BMP7*, *COLEC11*, and *DDR1* (11). The most prominent association signal was a missense variant in *COL4A3*, rs55703767 (Asp326Tyr), which affects type IV collagen, a key structural component of the glomerular basement membrane. Notably, the minor allele of this variant was associated with a protective effect against DKD, including reduced risk of albuminuria and ESRD, and was further correlated with decreased glomerular basement membrane thickness prior to the onset of clinically detectable kidney damage. A recent GWAS meta-analysis encompassing nearly 27,000 individuals with diabetes, using ten distinct DKD phenotypic definitions, uncovered a novel intronic variant rs72831309 in *TENM2*, which is associated with a reduced risk of both albuminuria and low estimated glomerular filtration rate (eGFR), and exhibits compartment-specific expression effects in kidney tissue (12).

Despite these achievements, current GWAS findings explain only a limited portion of DKD heritability. The limited explanatory power is likely due to the modest effect sizes of common genetic variants and the substantial phenotypic heterogeneity of DKD observed across individuals and populations (8). Increasing evidence indicates that rare and low-frequency variants typically overlooked by conventional GWAS approaches may have a more pronounced impact on disease susceptibility. In this context, next-generation sequencing (NGS) technologies, including whole-exome sequencing (WES) and whole-genome sequencing (WGS), present valuable tools for uncovering such variants, thereby offering deeper insights into the complex genetic architecture of DKD.

NGS has advanced the discovery of novel genetic variants linked to DKD, succeeding through both WGS and WES (13). WES is a genome-wide approach that selectively targets the protein-coding regions of the genome, which are particularly enriched for disease-associated variants (14). Compared to WGS, WES is considered more clinically applicable, as it focuses on nucleotide alterations within exonic regions that encode proteins, areas where the majority of pathogenic variants are typically located (14). A major advantage of WES lies in its ability to generate a more manageable volume of data compared to WGS, which facilitates interpretation while reducing computational demands and cost (14). Despite these benefits, WES can still detect upwards of 100,000 nucleotide variants per individual (15), highlighting the need for robust analytical strategies to distinguish truly pathogenic variants associated with disease phenotypes.

To classify a sequence variant as pathogenic or disease-associated, it should ideally be absent or extremely rare in unaffected control populations and should be predicted to result in a deleterious effect on protein structure or function. Establishing the clinical relevance of such variants is essential to elucidating their role in disease etiology. Both WGS and WES have contributed to the identification of novel biological pathways implicated in DKD pathogenesis, thereby creating a foundation for future therapeutic strategies that may target these pathways or correct underlying genetic defects (16). However, relatively few WES studies have been conducted specifically in DKD (13, 17), and its full po-

tential for diagnosis, risk stratification, and management remains underexplored. Nevertheless, WES holds promise not only for identifying novel etiologic variants related to DKD but also for detecting incidental, clinically actionable mutations that may inform broader aspects of patient care.

There is a growing imperative to undertake comprehensive and context-specific investigations into the pathogenesis of DKD. To date, genetic studies of DKD in Kazakhstan remain limited, despite the country's pronounced ethnic heterogeneity, which may yield distinct genetic profiles compared to populations previously studied. Expanding research efforts in such underrepresented settings is essential for translating genomic discoveries into clinically meaningful interventions and advancing precision medicine in DKD management. Future research should prioritize the inclusion of larger, multi-ethnic cohorts, alongside high-resolution fine-mapping strategies aimed at identifying causal variants. Moreover, the integration of genome-wide data with transcriptomic, proteomic, and metabolomic analyses holds considerable promise for elucidating critical molecular pathways and uncovering novel therapeutic targets.

Author Contributions: Conceptualization, A.S.-S., B.T.; methodology, B.T.; writing – original draft preparation, B.T.; writing – review and editing, A.S.-S., B.T., K.A., K.M. All authors have read and agreed to the published version of the manuscript.

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: This research was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan, grant number AP19676488.

Ethics approval: Not applicable

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Central Asian Journal of Nephrology

Case Report

A Case Report of a Diabetic Nephropathy Patient with Cirrhotic Ascites and HIV Recommended for Peritoneal Dialysis

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Abstract:

Received: July 30, 2025
Accepted: August 16, 2025

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A 46-year old male was admitted to the University Medical Center (UMC) hospital with the following symptoms of anuria, abdominal fullness, hypotension, exertional dyspnea, and peripheral edema. The purpose of his visit was the insertion of a peritoneal dialysis catheter. He had chronic kidney disease stage 5 as a consequence of diabetic nephropathy, liver cirrhosis due to hepatitis C infection, and HIV. His disease course was further complicated by the presence of a urinary tract infection. As a result of his multiple comorbidities, he underwent a complex treatment regimen which included renal replacement therapy with ultrafiltration, blood transfusions for his anemia, platelet transfusions for his thrombocytopenia, albumin infusion for his hypoalbuminemia, and antibiotic treatment for his concurrent infection. Additionally, he received diuretic treatment for his hypervolemia and anti-hypertensives to control his blood pressure. After peritoneal dialysis (PD) insertion, the patient successfully underwent PD and was discharged home.

Keywords: Diabetic Nephropathy; Cirrhotic Ascites; HIV Infection; Case Report; Renal Complications; Comorbidities; Chronic Kidney Disease; Liver Cirrhosis; Infectious Disease; Nephrology

Introduction

One of the most common and serious complications of type I Diabetes Mellitus (T1DM) is diabetic nephropathy. It mainly results from endothelial dysfunction and proinflammatory pathway activation leading to renal microvascular lesions (1, 2). Moreover, this complication develops in approximately 35% of type I Diabetes patients and often follows a progressive course, further advancing to albuminuria, declining glomerular filtration rate (GFR), and advancing to end-stage renal disease (ESRD) (3). While diabetic nephropathy is an established cause of chronic kidney disease (CKD), other comorbid conditions, particularly chronic viral infections such as HIV and hepatitis C can significantly impair kidney function.

In patients with an HIV infection, chronic inflammation and dysregulation in immune mediators can significantly contribute to kidney damage, often manifesting as HIV-associated nephropathy (HIVAN) (4). Additionally, antiretroviral therapy (ART), while essential, can have a nephrotoxic effect. Similarly, patients with hepatitis C infection are also prone to the exacerbation of CKD as it induces kidney injury by the formation of immune complexes and cryoglobulins (5). Additionally, chronic hepatitis C infection, being the leading cause of liver cirrhosis, can precipitate hepatorenal syndrome (HRS) resulting in vasodilation and diminished renal perfusion.

The following case study reports a patient with coexisting type I DM, HIV and hepatitis C infections. It

is highly likely that a cholinergic effect of these comorbidities accelerated the progression of CKD, further complicating his clinical management.

Case Report

A 46-year old male was admitted to the UMC hospital because of anuria, abdominal fullness, hypotension, exertional dyspnea, and peripheral edema. He was diagnosed with type 1 diabetes mellitus in 2007 and Essential hypertension stage 3 in 2019. Furthermore, in 2020, he was found to have liver cirrhosis as a result of chronic hepatitis C infection and tested positive for an HIV infection. Patient had an intravenous drug use history, which included shared use of needles and injection equipment. Thus, he associated his hepatitis C infection with the HIV acquisition risk. He received antiviral therapy consisting of Kivexa (Abacavir 600 mg + Lamivudine 300 mg) and sometimes Truvada (Tenofovir disoproxil fumarate 245 mg + Emtricitabine 200 mg) based on the availability of the medication in AIDS control center. In 2023 his blood results revealed azotemia. As a result, he was consulted by a nephrologist, who recommended an antihypertensive therapy. Additionally, all antihyperglycemic medications were discontinued. In April 2024 he was admitted to the hospital for the treatment of liver cirrhosis, where his GFR was detected to be 27 ml/min. In July 2024 he was admitted with the following complications: secondary hyperparathyroidism, hyperphosphatemia, and diabetic nephropathy (stage IV by Mogensen classification). Furthermore, he had essential hypertension (stage 3), liver cirrhosis (Child-Turcotte-Pugh class B), portal hypertension, ascites, hypersplenism, and hepatic encephalopathy (West Haven stage 1). Moreover, his GFR was reduced to 12.2 ml/min. In August 2024 he was admitted to the ICU for acute decompensation, presenting with reduced urination, worsening of edema, nausea, and vomiting. Lab analysis results showed increased creatinine (587 umol/L), azotemia (38 mmol/L), hyperkalemia (7.2), and metabolic acidosis (pH 7.181). Based on these clinical findings and anuria, he received 10 sessions of hemodialysis during his hospitalization. A multidisciplinary team meeting was held and it was decided to place the patient on peritoneal dialysis (PD). In September 2024, he was admitted on a planned basis to UMC for the insertion of a PD catheter.

Upon admission, physical examination showed ascites, peripheral edema, and jaundice. The patient was in respiratory distress and had hypotension (80/40 mm Hg). In order to rule out infection, septicemia, and shock due to sepsis, procalcitonin and C-reactive protein were measured. Moreover, blood, throat, nasopharyngeal, and urine cultures were taken. Laboratory studies demonstrated hemoglobin of 84 g/L, MCH of 28.10 pg, RBC of 2.99x1012/L, and platelets of 94.0x1012/L. Biochemistry analysis depicted a creatinine of 378.70 μmol/L, urea of 14.40 mmol/L, CRP of 23.80 mg/L, and albumin of 30 g/L. His GFR was 16 ml/min. His electrolytes were as follows: sodium - 134 mmol/L, potassium - 4.40 mmol/L, total calcium - 2.10 mmol/L, ionized calcium - 1.01 mmol/L, magnesium - 0.89 mmol/L and phosphate - 2.01 mmol/L. Procalcitonin level was within the normal range. His ABG indicated metabolic acidosis with a pH of 7.29 and BE (ecf) of 1.6 mmol/L. The urinalysis revealed leukocytes of 702 hpf, erythrocytes of 688.8 hpf, and protein of 2.10 g/L. Urine culture demonstrated the presence of Enterococcus faecalis of 50,000 CFU/ml. Her ultrasound confirmed ascites, liver cirrhosis, and portal hypertension, along with splenomegaly. Additionally, esophagogastroduodenoscopy was performed to rule out gastrointestinal bleeding and grade 3 esophageal varices were observed. Also, it is remarkable that patient's cardiac ejection fraction dropped to 57% in 2024%.

In order to address his hypervolemia and electrolyte derangements, continuous renal replacement therapy was performed with ultrafiltration at the rate of 500 ml/hour and anticoagulation using heparin (1000 IU/hour). Additionally, 20% albumin infusion was administered to manage his hypoalbuminemia (albumin level 26 g/L) which was contributing to his hypervolemia. Due to his worsening anemia (hemoglobin level 56 g/L), he received a transfusion with two doses of packed RBCs, along with epoetin beta. Furthermore, to reduce his risk of bleeding from thrombocytopenia (56x109/L), he underwent platelet transfusion twice. Based on his urinalysis and urine culture findings, which indicated Enterococcus faecalis, meropenem (1000 mg/day) was initiated to treat his urinary tract infection. Insertion of the PD catheter was performed via laparotomy under general anesthesia. Upon entering the abdominal cavity, a large amount of clear ascitic fluid was observed and 5 liters were aspirated. A Tenckhoff catheter for peritoneal dialysis was implanted into the pelvic cavity. It was then tunneled subcutaneously through the left mesogastrium and closed with a Betadine cap, after extension with a titanium adaptor. The next day after the procedure the patient continued to have oliguria (less than 100 ml) and he was placed on continuous renal replacement therapy.

The patient then began to undergo PD once every 24 hours with the following parameters - Physioneal® 40 (2.27% glucose concentration), Physioneal® 40 (1.36% glucose concentration), 4-hour dwell cycle, and a fill volume of 1500 mL per exchange. Compared to the results of his lab analyses on admission, his creatinine dropped to 357.66 μmol/L. However, his potassium level rose to 6.4 mmol/L and his sodium level dropped to 132 mmol/L. The patient continued to receive albumin infusion and upon discharge, his albumin level rose to 27.50 g/L (from 26.0 g/L) and his total protein was 50.0 g/L.

During his stay, he additionally received calcium gluconate to correct his hyperkalemia. Insulin was used to manage his hyperglycemia associated with diabetes. Also, furosemide was given for his fluid overload during the first 24h of hospitalization, which was changed to isolated ultrafiltration on the second day. In the days following the PD insertion procedure, carvedilol, amlodipine, and nifedipine were also administered to carefully control his blood pressure.

Discussion

A 46-year old male with CKD and multiple comorbidities such as HIV and hepatitis C infections, later developing urinary tract infection, was admitted for the PD catheter placement and further management.

As mentioned above, diabetic nephropathy is one of the most common and devastating complications of T1DM. Usually, it has a progressive course, which can be subtly divided into several stages according to Mogensen (6) with each having relatively specific patterns. During Stage 1, while renal hyperfunction and hypertrophy occur, these changes are, at least, partially reversible with an insulin treatment. In Stage 2, individuals usually do not exhibit clinical manifestations, however, kidney function tests can already demonstrate signs of disease. On the other hand, several patients can remain on this stage throughout their lives. Stage 3 is informally considered to be an initial phase of diabetic nephropathy, when albumin excretion level is abnormally elevated. This stage, however, can be slowly advancing over many years, during which, several patients can already develop hypertension. Subsequently, stage 4 is progressing to an overt nephropathy, characterized by a persistent proteinuria and a declining GFR. Finally, stage 5 is the ESRD with the patient having uremia and requiring renal replacement therapy.

In individuals with HIV, HIVAN can be a serious complication and can be observed in up to 17% of patients. Significant risk factors that increase the risk of renal damage in HIV patients are hepatitis C infection and diabetes, which both are present in the following patient. Moreover, exposure to ART can itself be a triggering factor for the decline in renal function (7). While there are a number of pathways responsible for the damage, intrarenal HIV gene expression is one of the mechanisms causing direct injury of the podocytes and glomerular scarring. Additionally, dysregulation in immune mediation and chronic inflammation also contribute to endothelial dysfunction and, as a result, renal fibrosis, further exacerbating the condition (8). Similarly, hepatitis C can significantly impair renal function by the precipitation of cryoglobulins which, in turn, cause mesangial inflammation and endothelial injury. Moreover, immune complexes can gather and deposit in the basement membrane, leading to glomerular damage and inflammation (9).

The patient's diabetic nephropathy compounded by his HIV and hepatitis C infection may have led to quicker progression of his disease (4,5) and led to the decompensated state observed in this patient. With a GFR of between 12.2-16 ml/min, metabolic acidosis (pH 7.181) and severe electrolyte derangements (hyperkalemia 7.2), the patient was in kidney failure and required immediate renal replacement therapy.

End stage renal disease in patients with multiple comorbidities as observed in this case present various challenges and must be individually tailored. For instance, treatment of hypervolemia in ESRD patients with cirrhotic ascites require careful monitoring as such patients often have low effective arterial volume despite being hypervolemic (10). Combined with the presence of coagulation abnormalities and malnutrition, cirrhotic patients do not tolerate the sudden removal of fluids from intravascular spaces well during intermittent hemodialysis (10). As such, peritoneal dialysis may offer a more hemodynamically stable alternative for our patient. Several reports exist that recommend PD for patients with liver diseases who have ascites (10,11). Studies by Chou et. al and Nadir et.al demonstrate that patients with kidney failure and cirrhosis on PD may have higher survival rates compared to groups on HD (12,13). A major advantage of PD is that anticoagulation is not required. Given that the coagulopathy observed in cirrhotic patients is often worsened by concurrent uremia, the potential reduction in the risk of bleeding is of significant importance. PD also removes the need for paracentesis as it allows constant drainage of ascites (7).

Nevertheless, certain complications need to be considered when performing PD such as the risk of infection, protein losses, pericatheter leaks and abdominal hernias. Despite these concerns, a study by De Vecchi et.al concluded that the risk of dialysis complications, including bacterial peritonitis, was not increased in cirrhotic patients receiving PD (14). However, given the presence of HIV, cirrhosis, diabetes, and coexisting infection, the risk of peritonitis, wound infection and sepsis were major concerns in our patient. Thus, using the antimicrobial resistance profile and the local resistance patterns as a guide, our patient received meropenem to treat his infection and prevent further progression. Given that PD is usually initiated two weeks post-insertion of a catheter to allow healing (15), the patient received continuous venovenous hemodiafiltration (CVVHDF) during his stay for the correction of his fluid overload and the prevention of electrolyte imbalances. CVVHDF presents an advantage over intermittent hemodialysis in our patient as it is considered to provide better hemodynamic stability (16). However, due to limited resources, and an inability to administer further hemodialysis due to the risk of HIV and hepatitis C transmission, the PD had to be initiated prematurely. To prevent the risk of leakage, a smaller fill volume of 1.5 L was used and the number of exchanges was limited to once per day. Consequently, hyperkalemia and hyponatremia were observed. However, these imbalances were expected to become normalized after the adjustment in the prescription of peritoneal dialysis once larger fill volumes could be used.

It is also noteworthy to mention that due to the presence of several underlying health conditions, a multidisciplinary approach had to be employed in the management of this patient. Firstly, the presence of cirrhosis in our patient complicated the management of his diabetes as loss of liver function can reduce insulin clearance. Therefore, the dosage of insulin had to be carefully administered to prevent hyperglycemia from his diabetes and hypoglycemia from his cirrhosis (17).

Secondly, the presence of hypervolemia in our patient could have been a consequence of both his cirrhosis and kidney failure. In either case, fluid overload is primarily treated with dietary sodium restriction and diuretic therapy, especially if there is residual renal function (18, 19). However, there are certain nuances that need to be taken into account. For example, diuretic resistance is frequently encountered in CKD patients. Furthermore, the choice of diuretic must be guided based on their excretion patterns. As furosemide is mainly excreted by the kidney, it would be the first choice in cirrhotic CKD patients whose kidney function is better preserved than their liver function. Similarly, torasemide is preferred in patients where kidney function is severely impaired (20).

Additionally, as PD is known to lead to increased protein losses, the already existing hypoalbuminemia in our patient due to his cirrhosis had to be carefully monitored. The patient received multiple albumin infusions as a part of his treatment plan. As a result, a drop in his albumin and total protein levels after PD was not observed. This highlights the importance of tailoring treatment strategies to address individual complications in patients with multiple morbidities.

The severe impairment of kidney function in this case underscores the value of an integrated approach when managing multiple chronic conditions. As his HIV and hepatitis C status might have exacerbated his kidney dysfunction, it is vital to ensure that in such patients comorbid conditions are being properly managed. Prompt treatment of HCV is essential to prevent liver-associated complications. In addition to that, antiretrovirals can be nephrotoxic and requires close monitoring. Thus, patient education to emphasize the significance of treatment adherence and regular follow-up is necessary to prevent progression of the chronic conditions, including CKD.

This case highlights several avenues for future research. Currently, no treatment guidelines exist for the management of patients with the combined diagnoses of diabetes, HIV, HCV, liver cirrhosis, and CKD. Thus, there is a need to optimize treatment protocols for such challenging patients. For instance, as regional hospitals often hesitate to provide hemodialysis to patients with HCV and HIV due to the risk of transmission of these viruses, a PD guideline tailored to cirrhotic patients could be established and implemented so that these patients can receive renal replacement therapy. This guideline should also include how patients should be selected for PD such as the consideration of socioeconomic conditions, compliance and mental capacity (which might be impaired in the case of hepatic encephalopathy) (15). Moreover, integrated care programs that address the unique challenges faced in patients with multiple chronic diseases should be developed by policymakers.

Conclusion

While PD is generally avoided in patients with cirrhosis and ascites due to the fear of higher risk of complications, current research indicates that this may not be the case. Thrombocytopenia and hemodynamic instability in these patients might even make PD the better choice. In our case report, we have presented a

patient with a unique set of comorbidities who successfully underwent the initiation of PD.

Author Contributions: Conceptualization, Z.K., A.K.; methodology, Z.K., M.M., L.T., V.A.; writing – original draft preparation, N.I., R.B.; writing – review and editing, B.A. All authors have read and agreed to the published version of the manuscript.

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: None.

Ethics approval: Not applicable.

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Central Asian Journal of Nephrology
(eISSN 3105-4145)

Short Communication

Integrating Novel Complement Inhibitors into Clinical Practice: A National Call to Action for C3 Glomerulopathy and IgA Nephropathy in Kazakhstan

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Abstract:

The advent of targeted complement inhibitors represents a paradigm shift in managing complement-mediated nephropathies. Integrating these therapies into healthcare systems, particularly in resource-variable settings, requires strategic planning.

A national council of experts was convened in October 2024 with the purpose of obtaining a clinical expert opinion to develop practical recommendations for improving the organization and optimization of medical care for patients with C3 glomerulopathy (C3G) and IgA nephropathy (IgAN) in Kazakhstan.

The council identified critical systemic gaps, including inconsistent use of renal biopsy, lack of specialized nephropathology, absence of treatment algorithms, and fragmented patient care. A consensus was reached on key recommendations for a new national clinical protocol. These include mandating pathological confirmation, creating detailed treatment and monitoring algorithms, establishing a national registry and coordination center, and investing in specialized training for healthcare professionals.

The systematic framework proposed by the council provides an actionable roadmap to overcome barriers to care. This model ensures equitable patient access to novel therapies

Received: August 27, 2025
Accepted: September 7, 2025
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and may serve as a blueprint for other nations navigating the integration of advanced treatments into clinical practice.

Keywords: C3 Glomerulopathy; IgA Nephropathy; Complement System; Targeted Therapy; Iptacopan; Clinical Protocol; Kazakhstan; Healthcare Policy

Introduction

C3 glomerulopathy (C3G) and IgA nephropathy (IgAN) are complex immune-mediated glomerular diseases where dysregulation of the alternative complement pathway is a key driver of inflammation and progression to end-stage renal disease (1, 2). For decades, management has relied on non-specific immunosuppression with variable efficacy and significant side-effect profiles. The recent development of targeted complement inhibitors, such as the oral factor B inhibitor iptacopan, has revolutionized the therapeutic landscape. Iptacopan has demonstrated significant efficacy in reducing proteinuria in patients with IgAN in the phase III APPLAUSE-IgAN trial (3) and has shown promising results in C3G (4,5), leading to recent regulatory approvals.

However, the integration of such highly specific, costly therapies into clinical practice presents significant challenges. In Kazakhstan, the absence of a unified national approach creates disparities in care and limits patient access. This short communication presents the consensus resolutions and strategic recommendations of a national expert council convened with the specific mandate to develop practical recommendations on:

- Improving the organization and optimization of medical care for C3G and IgAN;
- Assessing and improving the state of diagnostics and provision of effective treatment within the current therapeutic landscape;
- Creating and implementing effective patient routing algorithms involving interdisciplinary interaction.

THE COUNCIL'S DELIBERATIONS: IDENTIFYING SYSTEMIC BARRIERS

Guided by its core mandate, the expert council, comprising leading nephrologists, pathomorphologists, and healthcare administrators, highlighted several interconnected barriers that currently impede optimal care for patients with C3G and IgAN in Kazakhstan:

1. **Diagnostic Inconsistency and Quality:** The practice of renal biopsy is not uniformly mandated or accessible across the country. A definitive diagnosis of C3G requires immunohistochemical staining and often electron microscopy, expertise for which is concentrated in major urban centers, creating a significant bottleneck. This directly impacts the assessment of diagnostics and limits opportunities for effective treatment.
2. **Fragmented Care Pathways and Routing:** The absence of a standardized national algorithm for referral, diagnosis, treatment initiation, and long-term monitoring leads to delays and inconsistencies in management. There is no central entity to coordinate care for these complex patients, hindering interdisciplinary interaction and effective routing.
3. **Knowledge Gaps:** There is a recognized need for continuous medical education focused on the pathophysiology of complement-mediated diseases, the interpretation of pathological findings, and the practical management of novel therapies, including their safety profiles. This gap affects the overall organization and quality of care provided.
4. **Lack of Epidemiological Data:** Without a national registry, the prevalence, natural history, and outcomes of C3G and IgAN in

Kazakhstan remain unknown, hindering public health planning, resource allocation, and the optimization of care systems.

5. **Therapeutic Access Barriers:** Even with drugs becoming available, the lack of a clear protocol for prerequisite vaccinations (e.g., against meningococci), monitoring for adverse events, and criteria for therapy initiation and continuation poses a significant risk of inequitable access and limits the provision of high-quality, effective treatment.

KEY RECOMMENDATIONS FOR A NATIONAL PROTOCOL

To systematically address these challenges and fulfill its mandate, the council formulated the following core recommendations to be enshrined in the new national clinical protocol:

1. **Mandatory Pathological Diagnosis:** Institute **mandatory renal biopsy** with a specialist nephropathology review as a non-negotiable standard for confirming the diagnosis of C3G and for risk stratification in IgAN before considering targeted therapy. This is the critical first step in improving diagnostic standards.
2. **Structured Treatment and Routing Algorithms:** Develop a detailed, step-by-step national algorithm that covers:
    - **Patient Workup and Routing:** Standardized pre-therapy screening and clear referral pathways to ensure interdisciplinary interaction.
    - **Therapy Initiation:** Clear criteria based on proteinuria and eGFR thresholds for starting targeted therapy.
    - **Monitoring and Dispensary Observation:** Protocols for assessing efficacy (reduction in proteinuria), safety (monitoring for infection), and long-term follow-up.
3. **Establish a National Registry and Coordination Center:** Create a **national registry** for C3G and IgAN, integrated with the existing DAMU MED electronic healthcare portal. This should be managed by a designated **Coordination Center** (e.g., based at the National Kidney Fund) to track patients, oversee care quality, facilitate research, and improve the overall organization of care.
4. **Investment in Specialist Capacity Building:** Launch a dedicated national educational program featuring:
    - **Pathologist Training:** Scholarships and partnerships for the training of pathomorphologists in specialized nephropathology techniques.
    - **Nephrologist Education:** Regular workshops and teleconferences on the practical management of complement-mediated diseases and novel therapeutics to optimize treatment provision.
5. **Consideration for Orphan Disease Status:** Advocate for the official recognition of C3G as an orphan disease within Kazakhstan to streamline access to dedicated resources and funded therapies, addressing the challenge of limited therapeutic options.

Conclusion

The arrival of targeted complement therapy necessitates an evolution from fragmented care to a coordinated, system-wide approach. The recommendations put forth by this expert council provide a comprehensive and actionable framework to modernize the management of C3G and IgAN in Kazakhstan. By focusing on accurate diagnosis, centralized coordination, continuous education, and systematic monitoring, this framework directly addresses the initial mandate of improving care organization, optimizing diagnostics and treatment, and implementing effective patient routing. This initiative ensures that breakthroughs in medical science translate equitably into improved patient outcomes and

may serve as a valuable model for other healthcare systems embarking on a similar journey.

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: The authors would like to thank all participants of the expert council for their valuable contributions. This communication reflects the consensus view of the council.

Funding: None.

Ethics approval: Not applicable.

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